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REMARKS

I. Status of the Application.

Claims 1 through 19 were pending in the original application (the "present application"). In a non-final Office Action dated May 6, 2006 (the "Office Action"), Examiner Eric Olson: (1) rejected Claims 1-3 and 5-19 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention; (2) rejected claims 14-15 under 35 U.S.C. § 102 as being anticipated by U.S. Patent No. 6,551,612 to Benowitz et al. (the "Benowitz Patent" or "Benowitz") and PCT International Publication WO01/08691 to Baranowitz (the "Baranowitz Reference" or "Baranowitz"); (3) rejected claims 1-4, 7-8, 10-13, and 16-19 under 35 U.S.C. § 103 as being obvious over Benowitz in light of U.S. Patent No. 4,919,140 to Richard Borgens (the "Borgens Reference" or "Borgens"); (4) rejected claims 1-4, 7-8, 10-13, and 16-19 under 35 U.S.C. § 103 as being obvious over Benowitz in light of U.S. Patent No. 4,919,140 to Richard Borgens (the "Borgens Patent" or "Borgens").

The Applicants appreciate meeting with Examiner Olson and Supervisory Examiner Jiang during the Examiner Interview of July 27, 2006. In response to the Office Action, and pursuant to the discussion with the examiners during the Examiner Interview, the Applicants hereby respectfully: (1) amend the claims to remove the phrase "or analog thereof" per the examiner's recommendation to overcome the rejection under 35 U.S.C. § 112, second paragraph; (2) cancel claims 14-15, without prejudice to overcome the rejection under 35 U.S.C. § 102; (3) amend independent claims 1 and 13 to overcome the examiner's rejections with regard to the obviousness rejections under 35 U.S.C. § 103 with regard to Benowitz, Borgens, and Baranowitz (collectively, the "Cited References"); (4) cancel claims 3, 7, 11, and 14-19 and submit new

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claims 20-29 in light of the topics discussed in the Examiner's Interview; and (5) submit the enclosed declaration clarifying the discussion of synergistic effects discussed in the application and inquired about by the Examiners. Finally, per the examiner's request, the Applicants are submitting a copy of the Request for Correction of Inventorship as previously submitted on August 30, 2005, along with the return postcard confirming receipt by the USPTO. Applicants respectfully request reconsideration of the pending claims in view of the following remarks.

II. Overview of the Cited References

A. The Benowitz Reference

The Benowitz Reference discloses a method for treating a central nervous system injury by modulating axonal outgrowth of central nervous system neurons after a non-chronic central nervous system injury, provided that the method can be performed within the first 100 hours after the acute injury has been performed on the performing a medical procedure. Abstract; col. 5, lns. 31-63; col. 8, lns. 19-22; col. 8, lns. 53-65. Exemplary embodiments disclosed in the Benowitz Reference discuss the use and study of inosine to help grow both goldfish and rat retinal ganglionic cells in vitro on a defined medium. Examples I-XI. However, the Benowitz Reference does not teach the use of inosine to generate spinal cord growth more than 100 hours after a spinal cord injury, nor does it teach the use of inosine to treat a chronic spinal cord injury.

B. The Baranowitz Reference

The Baranowitz Reference discloses methods for transdifferentiating body tissues which can be used to generate specific cell types needed for replacement of organs or body parts. Abstract. More specifically, the Baranowitz Reference teaches a method for causing differentiated cells to revert to pluripotent cells by submitting the cells to trauma, an effective amount of a transdifferentiating agent (including guanosine); and the use of an effective amount

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of a stabilizing and differentiating agent (such as riboflavin, beta-carotene, etc.). In one example, the Baranowitz Reference discusses a method for identifying novel compounds that possess transdifferentiation and/or stabilization capacity by treating a melanocyte and observing it to see whether it transdifferentiates into a neuron. Therefore, the Baranowitz Reference discloses a method of causing differentiated cells to dedifferentiate and to thereafter redifferentiate into another type of cell, and does not disclose a method for treating a spinal cord injury or restoration of nerve function.

C. The Borgens Reference.

The Borgens Reference, as discussed in the Background section of the present application, discloses the use of oscillating field stimulation to cause nerves in the central nervous system of a mammal to regenerate. Abstract. However, as discussed in the Background of the present application, the use of oscillating field stimulation alone was shown to be effective in treating acute injuries only when administered within three weeks of the injury to the central nervous system. Page 2, lns. 5-7. As further stated in the Background, oscillating field stimulation alone was found to be ineffective in the regeneration of chronically injured tissue. Page 2, lns. 7-12.

III. The Amended Claims Are Not Indefinite

The examiner originally rejected claims 1-3 and 5-19 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Specifically, the examiner indicated that the language as claimed recited a "purine nucleoside or analog thereof," noting that the language "or analog thereof" does not clearly and distinctly indicate which molecules are claimed. In response, the Applicants have amended the claim language to remove the phrase "or analog thereof," thereby removing the

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basis for a rejection under 35 U.S.C. § 112, second paragraph. Applicants submit that the claims as amended are allowable, and respectfully request allowance of those claims.

IV. Claims 14 and 15 Have Been Cancelled

In response to Examiner Olson's rejection of claims 14 and 15 under 35 U.S.C. §102, Applicants have cancelled claims 14 and 15, but reserve the right to introduce these claims in a future continuation application. As such, Applicants believe that the Examiner's rejection has been addressed, and respectfully request that the remaining claims be allowed.

V. Amended Claim 1 Should Be Allowed.

The examiner initially refused independent claim 1 under 35 U.S.C. §103, indicating that claim 1 was obvious with respect to Benowitz in view of Borgens, and with respect to Baranowitz in view of Borgens. Applicants have amended independent claim 1 to further define the scope of the claims, and respectfully request allowance of independent claim 1 in light of the following remarks.

A. Amended Claim 1 is not Obvious

Applicants hereby submit that amended independent claim 1 should be allowed in light of the unexpected results and synergistic effects discussed in the present application and in the enclosed Rule 132 Declaration. The Court of Appeals for the Federal Circuit (the "Federal Circuit") has held that a combination of existing elements that produces a greater than expected result serves as evidence of nonobviousness. *In re Corkhill*, 711 F.2d 1496 (Fed. Cir. 1985); MPEP 716.02(a). In addition, evidence of greater than expected results when two previously known elements are combined ("synergism") is also evidence of nonobviousness. *Merck & Co. Inc. v. Biocraft Laboratories, Inc.*, 874 F.2d 804 (Fed. Cir. 1989). While synergism alone does not require a finding of nonobviousness if synergism is taught in the prior art, unexpected results

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greater than those which would have been expected based upon the prior art teachings indicate nonobviousness. *See Ex parte The NutraSweet Co.*, 19 USPQ2d 1586 (BPAI 1991). Further, presence of a property not possessed by the prior art is evidence of nonobviousness. *In re Papesch*, 315 F.2d 381 (CCPA 1963)(claims to compound structurally similar to prior art compound reversed due to unexpected anti-inflammatory properties not possessed by prior art compound). Therefore, in light of the evidence presented in Applicants' Rule 132 Declaration, Applicants submit that independent claim 1 is patentable due to the unexpected results and properties not possessed by the Cited References either alone or in combination.

Just as unexpected results and properties of a claimed invention supported the finding of nonobviousness in the *Papesch* and *Corkhill* cases, Applicants respectfully submit that the synergisms and unexpected results from the combination of limitations of claim 1 compel a finding that claim 1 is not obvious in light of the Cited References. Specifically, as noted in Examiner Olson's discussion of the cited references, the Benowitz reference teaches that a pharmaceutical composition comprising inosine should be administered intrathecally, and the method of treatment taught is "further limited to administration of the pharmaceutical composition, 'from the time of the spinal cord injury to 100 hours after the spinal cord injury.'" Office Action, Page 5, ¶ 3. Further, Benowitz teaches the use of inosine only in non-chronic injuries and gives examples of treatment of fish and rat retinal ganglionic tissue only. Likewise, as discussed in the Background section of the present application, while the method disclosed in the Borgens Patent has been shown to cause regeneration of axons and dendrites in the central nervous system of a mammal, the use of oscillating field stimulation alone has been shown to be effective in treating acute injuries only when administered within three weeks of the injury to the

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central nervous system. Page 2, lns. 5-7. Further, oscillating field stimulation alone was found to be ineffective in the regeneration of chronically injured tissue. Page 2, lns. 7-12.

Therefore, given the temporal limitations inherent in the treatments discussed in the Benowitz and Borgens Patents, as well as the apparent ineffectiveness of the methods to treat chronic spinal cord treatments, Applicants submit that the results of the method of claim 1 as discussed in the enclosed Rule 132 Declaration and in the present application show results that would not be expected based on the prior art disclosures and limitations inherent therein. Specifically, there is no indication in the art that combining the methods disclosed in the Borgens and Benowitz Patents would allow for successful treatment of chronic injuries, nor is there a suggestion that combining the methods disclosed in the Benowitz and Borgens Patents would allow for successful treatment of acute injuries more than 100 hours or 3 weeks post injury, respectively. Therefore, for the reasons set forth above, it is submitted that amended claim 1 overcomes the examiner's rejection under 35 U.S.C. §103 with regard to Benowitz in view of Borgens because the combination of the two elements results in a method that displays properties not present in the individual methods when practiced alone. Applicants respectfully submit that in light of the synergistic and unexpected results described and disclosed in both the present application and the Rule 132 Declaration, as well as the properties present in the combination that are not present in either method separately, claim 1 is not obvious with respect to Benowitz in view of Borgens. Applicants respectfully request allowance of claim 1.

B. Amended Claim 1 is not Obvious.

Applicants respectfully submit that the Examiner's rejections of Claim 1 under 35 U.S.C. § 103(a) should be withdrawn because the Examiner has failed to establish a *prima facie* case of obviousness in support of this rejection. Three criteria must be met to establish a *prima facie*

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case of obviousness: (i) there must be some suggestion or motivation to combine the teachings of two or more prior art references; (ii) there must be a reasonable expectation of success; and (iii) the prior art references, when combined, must teach all the claim limitations. MPEP § 2143. In this instance, Applicants respectfully contend that the examiner has failed to make a prima facie case of obviousness because (1) there is no motivation to combine the references, (2) there is no reasonable expectation of success in combining the two references, and (3) the combination of the references does not include all the limitations of independent claim 1.

The examiner indicated that claim 1 is obvious with regard to Baranowitz in light of Borgens because Baranowitz teaches a treatment capable of regenerating tissues and organs through dedifferentiating mammalian cells. The method disclosed in Baranowitz involves the use of trauma and the administration of guanosine (a purine nucleoside) to allow transdifferentiation to occur. The examiner indicated that when it is considered that spinal tissue is within the range of tissues that can be produced through transdifferentiation, and the method of Borgens is used as a backdrop, every element of claim 1 is disclosed and claim 1 is rendered obvious.

However, as discussed in the Rule 132 Declaration, the addition of neurons to the site of a spinal cord injury is widely held to have no effect on restoration of nerve function. Declaration, ¶3-6. Rather, spinal cord injuries that produce functional loss are the result of damage to the axons and dendrites that comprise white matter. *Id.* Thus, even if the practice of transdifferentiation taught in Baranowitz is followed and neurons are created from endothelial cells to populate an area of spinal cord injury, there is no expectation that such a treatment would cause regeneration of white matter (axons and dendrites) that would at least partially restore nerve function. Further, as discussed in the present application and in the attached Rule 132

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Declaration, testing has shown that neural regeneration and at least partial restoration of nerve function occurs due to stimulation of growth of the axons and dendrites of existing neurons. No indication of increased population of neurons has been noted in effective treatments.

A reference is non-analogous art if: (i) the reference is not "within the field of the inventor's endeavor," and (ii) the reference is not reasonably pertinent to the particular problem with which the inventor was involved. See *In re Deminski*, 796 F.2d 436 (C.A.F.C. 1986). Therefore, since the Baranowitz Reference teaches a method for the creation of cells that are not known to have any therapeutic function in restoration of spinal cord function in a spinal cord injury, Applicants submit that the Baranowitz Reference is nonanalogous art with respect to the present application.

Further, since the mechanism for restoration of nerve function in an injured spinal cord is through the regeneration or growth of axons and dendrites on existing neurons within the spinal cord, the Applicants note that there is no expectation of success in combining the transdifferentiation method of Baranowitz with the method of the Borgens Patent. There is no evidence in the art to believe that such a combination would result in restoration of nerve function. Declaration, ¶ 6. Therefore, since transdifferentiation is not expected to play a part in restoration of neural function in a spinal cord injury, there would be no motivation to combine the two references by one of ordinary skill in the art. Additionally, as discussed above, there would be no expectation of success even if the two methods were combined.

Finally, Applicants note that independent claim 1 includes the limitation of "wherein nerve function through said injured spinal cord is at least partially restored." There is currently no evidence that the use of OFS with the method described in Baranowitz would result in at least partial restoration of nerve function in an injured spinal cord. Therefore, Applicants submit that

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even when the Baranowitz Reference is read in view of the Borgens Patent, each and every limitation of independent claim 1 is not disclosed. For these reasons, Applicants submit that a *prima facie* case of obviousness has not been made with regard to claim 1 with respect to Baranowitz and Borgens, and reconsideration is respectfully requested.

VI. The Rejection of Independent Claim 13 under 35 U.S.C. § 103 (a) Should be Withdrawn.

The Examiner initially rejected independent claim 13 under 35 U.S.C. § 103(a) as being obvious over Benowitz in view of Borgens, or over Baranowitz in view of Borgens. Applicants respectfully submit that the Examiner's rejections of Claim 1 under 35 U.S.C. § 103(a) should be withdrawn because the Examiner has failed to establish a *prima facie* case of obviousness. As discussed above, and noted by the examiner in the Office Action, Three criteria must be met to establish a *prima facie* case of obviousness: (i) there must be some suggestion or motivation to combine the teachings of two or more prior art references; (ii) there must be a reasonable expectation of success; and (iii) the prior art references, when combined, must teach all the claim limitations. MPEP § 2143. Further, the application of hindsight to support a rejection under 35 U.S.C. § 103(a) is not permitted under the law. See, e.g., In re Rouffet, 149 F.3d 1350 (Fed. Cir. 1998). Applicants contend that the amended claims are not obvious, as (1) the Cited References do not contain all of the limitations of claim 13, (2) there would be no motivation to combine the references at the time of the invention, (3) there would be no reasonable expectation of success at the time of the invention, and (4) the Baranowitz reference is nonanalogous art.

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A. The Baranowitz Reference in Light of Borgens Does Not Render Claim 13

Obvious

Applicants respectfully renew their objection with regard to the citation of the Baranowitz Reference, noting that the Baranowitz Reference is not analogous art. Further, for the reasons set forth above in Section V(B), Applicants submit that there exists no motivation for combining the Baranowitz Reference with the Borgens Patent, to achieve the desired result of treating a spinal cord injury. Further, there is no reason to expect that such a combination would be successful. In addition, Applicants note that amended claim 13 includes the limitation of "electrically stimulating the site of a chronic spinal cord injury through the use of oscillating field stimulation." As discussed above and in the present application, use of the method disclosed in the Borgens Patent alone was known to be ineffective in treatment of a chronic spinal cord injury, and there is no discussion of treatment of chronic spinal cord injuries in the Baranowitz Patent. Therefore, it is respectfully submitted that the cited references do not contain each and every limitation of amended claim 13.

B. The Benowitz Reference in Light of Borgens Does Not Render Claim 13

Obvious

Applicants respectfully incorporate their discussion and arguments presented in Section V(A), and submit that amended claim 13 is not obvious over Benowitz in view of Borgens for the same reasons. Specifically, it is noted that amended claim 13 utilizes the steps of claim 1 to treat a chronic spinal cord injury, "wherein nerve regeneration at the site of the chronic spinal cord injury is stimulated." Therefore, in addition to the previously presented discussion regarding unexpected results and synergisms, applicants submit that the examiner has failed to establish a prima facie case of obviousness because (1) Benowitz in light of Borgens does not

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contain all of the limitations of claim 13, (2) there would be no motivation to combine the references at the time of the invention, and (3) there would be no reasonable expectation of success at the time of the invention.

As noted in the overview of references cited and in the examiner's discussion of the art, Benowitz teaches the use of inosine to treat an acute spinal cord injury if applied within the first 100 hours after injury. Similarly, the method disclosed in the Borgens Patent was shown to be effective in treating acute injuries if administered to patients within 3 weeks of injury, but was shown to be ineffective when applied in chronic spinal cord injuries. Amended claim 13 includes the limitation of treatment of a chronic spinal cord injury, which is not disclosed in either Benowitz or the Borgens Patent. Therefore, Applicants submit that the references cited do not teach every limitation of amended claim 13.

Further, it is documented that the method disclosed in the Borgens Patent is not effective in treating chronic spinal cord injuries, and the Benowitz Patent teaches that the treatment finds efficacy only in acute injuries within 100 hours of the injury. In light of these shortcomings in the prior references, Applicants respectfully submit that there would be no motivation to combine two methods that are documented to be ineffective in treatment of chronic spinal cord injuries in order to treat a chronic spinal cord injury. Further, since the method of the Borgens Patent has been shown ineffective with regard to chronic injuries, and the Benowitz Patent likewise teaches effectiveness only in non-chronic injuries within 100 hours of the injury, Applicants submit that there was no reasonable expectation of success in combining the two references to treat chronic spinal cord injuries.

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A. The Rejection of the Remaining Claims Under 35 U.S.C. § 103(a) Should be Withdrawn

The remaining claims depend from amended independent claims 1, 13, and 25. Since neither independent claim 1 or independent claim 13 are obvious in light of the Cited References, the claims depending therefrom cannot be anticipated by the Cited References. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejections of the remaining claims.

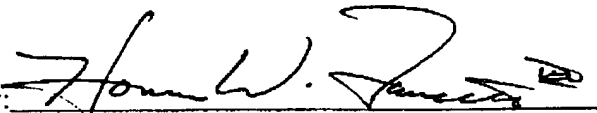
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VII. Conclusion

For all the foregoing reasons, it is respectfully submitted that the Applicants have made a patentable contribution to the art and that this response places the above identified application in condition for allowance, or in the alternative this response places the application in a better form for appeal. Favorable reconsideration and allowance of this application is respectfully requested. Should the Examiner continue to find any of the Claims objectionable for any reason, the Examiner is respectfully requested to contact the undersigned for a telephone interview before taking further action. The original application contained 3 independent claims and 19 total claims. As amended, the present application contains 3 independent claims and 21 total claims. Applicants authorize payment of the \$25 for the additional claim in excess of 20 to be charged to deposit account 09-0007. In the event the Applicants have inadvertently overlooked the need for an extension of time or payment of an additional fee, the Applicants conditionally petition therefor, and authorize any fee deficiency to be charged to deposit account 09-0007.

Respectfully submitted,

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Encl: Facsimile Cover Sheet
Rule 132 Declaration
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